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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,887	03/05/2002	Benjamin Eithan Reubinoff	13164A	7135

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,887	REUBINOFF ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed March 5, 2002, is a divisional of 09/436,164, filed November 9, 1999, which claims benefit of foreign applications PP7009, filed November 9, 1998, and PQ2852, filed September 15, 1999, both filed in Australia.

Applicants' amendment filed November 26, 2004, has been received and entered. Claims 1-32 and 35 have been canceled. Claims 33 and 36 have been amended. Claims 37 and 38 have been added. Claims 33, 34 and 36-38 are pending and currently under examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 36 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-26, 38-44, 47-55 of copending Application No. 09/436,164 is withdrawn.

It is noted that 09/436,164 has gone to issuance (US Patent Number not assigned). Upon consideration of Applicants' arguments and review of the allowed claims in 09/436,164,

Examiner agrees that the claimed inventions drawn to different methods are distinct. Further, while 09/436,164 results in a stem cell line, there are no specific steps recited in the allowed claims that indicate that the resulting stem cells are vitrified or frozen by any manner. Though claim 36 of the instant application does not require the claimed stem cell line to be frozen (because Example 6 teaches frozen and thawed stem cells), the methods of 09/436,164 would result in a differentiated stem cell, not a stem cell line as required by claim 36.

Claim Objections

Claims 37 and 38 are objected to because of the following informalities:

Newly added claims 37 and 38 set forth embodiments encompassing "hES" cell(s), and while generally supported in the present disclosure as the acronym of human embryonic stem cell, HES is also used in naming specific stem cell lines (see for example page 37--HES-1 cell line used in working example). When not specifically defined in the specification, the first presentation of an abbreviated term should be denoted by setting forth the full name indicating the term to be used subsequently.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to the claims is noted, however review of Example 6 indicates that it is not a method for making human embryonic stem cell lines, but rather a method for cryo-preserving a cell. Moreover, following the specific working example the specification makes the statement "that various modifications and/or alterations may be made without departing from the spirit of the present invention" (bottom of page 37), without clearly setting forth what the "spirit" of the invention is. More importantly, the specification clearly teaches that the methods of vitrification contemplated and used were those known in the prior art (see for example page 30).

Applicants argue that the specification describes human stem cell lines, and point to Example 6 where HES-1 is specifically used in the working example. See Applicants amendment, page 5. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, though claim 36 specifically refers to Example 6, the title of Example 6 clearly indicates that it is a method of "Cryo-preservation of human ES cells" (see title), not a method of making or preparing human ES cells. Further, it is noted that it does not exclude modifications to the method specifically set forth in the example, therefor even the reference to a specific example is non-limiting. Referring to an example that is non-limiting renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). It is important to note that the methods of cryopreserving a cell contemplated and used in the instant specification are not new and

specfically refer to those disclosed by Vajta *et al.*, see reference made in Example 6, page 37. Also, human embryonic stem cells are not new, and that the example uses an established cell line, not one created with any of the methods disclosed in the instant application. To this end, the claim appears to be incomplete because it omits essential elements, such omission of what parts of Example 6 are to be considered in preparing the stem cell line, and what is considered Applicants' invention. See MPEP § 2172.01. Again, the methods of freezing contemplated and human embryonic stem cells were known in the prior art. Example 6 appears to be only a method of freezing stem cells with known methods. There is no specific disclosure for methods of making human embryonic stem cells, and while it is generally set forth the cells are propagated, there is no specific methodology in the example to how either of these are accomplished. It is maintained that claim 36 is indefinite because while the claim has been amended to indicate a specific working example, the specific method(s) in Example 6 can not be used to make human embryonic stem cells lacking essential steps, therefor fails to clearly set forth what is encompassed by the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 36 stands rejected and newly added claims 37 and 38 are rejected under 35 U.S.C. 102(b) as being anticipate by Thomson *et al.* (Science 282:1145-1147-IDS Reference).

Applicants summarize the basis of the rejection and note that claim 36 now requires that the cell line be prepared by the methods set forth in Example 6. Applicants argue that the claimed composition can be distinguished from that disclosed by Thomson *et al.* See Applicants amendment, pages 5-6. Applicants' arguments have been fully considered, but not found persuasive.

Initially, it is noted that Example 6 teaches frozen and propagating stem cells. To this end, the isolation and propagating human embryonic stem cell lines taught by Thomson *et al.* still anticipate the claims. Newly added claim 37 simply requires that the cell is cryopreserved, and claim 38 is a product by process that refers to the method of claim 33, requiring at most that the cell is vitrified. Each of the new claims, and claim 36 to the extent it encompasses methods of freezing a cell disclosed in Example 6, can reasonably be interpreted to be a cryopreserved composition of human embryonic stem cells. Thomson *et al.* teaches that the cell lines disclosed in the reference were cryopreserved (see for example second paragraph), and that after freezing the cell lines could be propagated without any apparent affect on the pluripotential characteristics of the cells. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its

fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972)

The claims encompass a human embryonic stem cell and/or wherein the stem cell line is cryopreserved. The claims can reasonably interpreted as an embryonic cell(s) isolated by any manner. As stated in the previous office action, Thomson *et al.* teach human pluripotent embryonic cell lines. Thomson *et al.* teach three cell lines: H13 and H14 which have a normal XY karyotype and H7 which has a normal XX karyotype (page 1145; second column). Thomson *et al.* teach that when the cell lines are injected into an immunodeficient mouse the cell lines can differentiate into endoderm, mesoderm and ectoderm cell types (page 1146; middle of first column and page 1147; figure 4). Further, characterization of the lines in culture, differentiation of the cells results in various cell types, including neuronal cells (neural epithelium shown in figure 4B). In characterizing the stem cell lines, various culturing methods were used to differentiate the cell lines. Among the parameters taught to affect differentiation of the cell lines was the feeder layer, the cell density, and various growth factors. With respect to the new embodiments that the cell is cryopreserved, Thomson *et al.* teaches that the cell lines disclosed in the reference were cryopreserved, and that freezing had no apparent affect on the pluripotential characteristics of the thawed cells.

In view of the breadth and lack of clarity of the claimed methodology the methods and general teachings of Thomosn *et al.* describing methods to stimulate or allowing the cell lines to differentiate in culture, anticipate the methods set forth in the instant claims.

Claim 36 stands rejected and newly added claims 37 and 38 are rejected under 35 U.S.C. 102(e) as being anticipate by Thomson (US Patent 6,200,806-IDS Reference).

Applicants argue that Thomson *et al.* does not disclose the methods set forth in Example 6, nor cells that cryopreserved, as required by the instant claims. See Applicants amendment, page 6. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, Example 6 teaches frozen and propagating cells, and to this end, the isolation and propagating human embryonic stem cell lines taught by Thomson *et al.* still anticipate the claims. Claim 37 simply requires that the cell is cryopreserved, and claim 38 is a product by process that refers to the method of claim 33, requiring at most that the cell is vitrified. Each of the new claims and claim 36 (to the extent it encompasses methods of freezing a cell disclosed in Example 6) can reasonably be interpreted to be a cryopreserved composition of human embryonic stem cells. Thomson *et al.* teaches that the cell lines disclosed in the reference were cryopreserved (see for example second paragraph), and that after freezing the cell lines could be propagated without any apparent affect on the pluripotential characteristics of the cells. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare

prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972)

The claims encompass a human embryonic stem cell and/or wherein the stem cell line is cryopreserved. The claims can reasonably interpreted as an embryonic cell(s) isolated by any manner. As stated in the previous office action, Thomson teaches a purified preparation of pluripotent human embryonic stem cells which are capable of differentiating into derivatives of the endoderm, mesoderm and ectoderm. Again, in the characterization of the cells it is demonstrated that the cells can differentiate into neural cells (column 11; lines 31-32). Further, conditions to culture the cells in gelatin treated culture plates is taught when placed in culture and allowed to grow for two weeks after achieving confluence, or grown without a fibroblast feeder layer the cells spontaneously differentiate (description in paragraphs bridging columns 14-15 and in Figure 6). Finally, Thomson teaches that the isolated cells can be cryopreserved and thawed without affecting the pluripotential characteristics of the cells.

Thus, the differentiated human cells and methods to differentiate said cells from pluripotent embryonic cells taught in Thomson *et al.* anticipate the claims.

Claims 33 and 34 stand rejected under 35 U.S.C. 102(b) as being anticipate by Vajta *et al.* (Acta Vet Scan, 1997 or Mol Reprod Dev, 1998-IDS reference).

Applicants note the amendment to claim 33 and summarize what the claims encompass. Summarizing the basis of the rejection, Applicants argue that Vajta *et al.* does not teach to use the method on human cells as required by the amended claims. See Applicants' amendment, pages 6-7. Applicants' arguments have been fully considered, but not found persuasive.

The amendment to claim 33 is noted. The claim encompasses a method of preserving a differentiated or undifferentiated cell, and dependent claim 34 still simply requires that the open pulled straw method of freezing be used. It is noted that the claim now requires that a human cell is frozen, not any animal as previously encompassed by the claims. However, Vajta *et al.* clearly teach that the disclosed methods can be used for humans as well (see for example summary in abstract). The method set forth in claim 33 has one simple step requiring the cell undergoes vitrification. Further, an embryo can be considered cells differentiated from embryonic stem cells, therefor the teachings of Vajta *et al.* to use the methods to cryopreserve human embryos anticipates the instant claims. The claims recite and encompass practicing the method with differentiated or undifferentiated cells, and the instant specification clearly teaches that the methodology contemplated is not new and refers to the methods taught by Vajta *et al.* Since the claims encompass practicing the method on any cell type, and since Vajta *et al.* disclose using the methodology on human embryos, the teaching of Vajta *et al.* anticipate the claims. The specification makes specific reference to Vajta *et al.* (1998) (page 25, lines 2-4). Vajta *et al.* (1998) as a prior art reference that teaches the Open Pulled Straw method for the vitrification of ova and embryos which represent differentiated and undifferentiated cell types.

Conclusion

No claim is allowed.

As noted previously, the methods of cryopreserving a cell contemplated and used in the instant specification are not new and specfically refer to those disclosed by Vajta *et al.* Further, while Vajta *et al.* teaches generally that the method can be used in preserving undifferentiated embryonic cells (*i.e.* frozen embryos), Reubinoff *et al.* (Hum Reprod 16(10):2187-2194) teach

that this method, the Open pulled Straw method for the vitrification of cells, can be successfully used in cryopreserving undifferentiated stem cells. Importanly, as suggested in the present specification, it is taught that the method does not result in any modification of the cells that are frozen, thus the methods of freezing would not provide a product that is distinguishable from that with which one started.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach